UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/967,030	09/27/2001	Randy H. Ziegler	25863.00120	4807

28983 7590 09/10/2002

CROSBY HEAFEY ROACH & MAY
1901 AVENUE OF THE STARS, SUITE 700
LOS ANGELES, CA 90067

EXAMINER
PATTEN, PATRICIA A

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 09/10/2002 7

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No.	Applicant(s)	
	09/967,030	ZIEGLER, RANDY H.	
	Examiner	Art Unit	
	Patricia A Patten	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 11-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-5, drawn to a composition comprising an extract of Brickellia, classified in class 424, subclass 725 for example.

II. Claims 6-7, drawn to a method for treating diabetes comprising an aqueous extract of Brickellia, classified in class 424, subclass 773 for example.

III. Claims 8-10, drawn to a method for treating diabetes via administration of a flavonoid such as luteolin, classified in class 252, subclass 182.31 for example.

IV. Claims 11-13, drawn to a method of controlling diabetes via administration of a molecule that binds to K_v 1.3 ion channels, classified in class 530, subclass 388.22 for example.

V. Claim 14, drawn to a method for controlling unwanted proliferation to T-cells in a mammal via administration of a molecule that binds to Kv 1.3 ion channels, classified in class 514, subclass 211.07 for example.

VI. Claim 15, drawn to a method of screening a group of compounds for anti-diabetic activity in a mammal, classified in class 436, subclass 501 for example.

VII. Claim 16, drawn to a method for screening a group of compounds for ability to suppress autoimmune responses in a mammal, classified in class 436 , subclass 503 for example.

VIII. Claim 17, drawn to a compound that contrails (sic) diabetes wherein the compound binds to and blocks Kv 1.3 ion channels, classified in class 514, subclass 307 for example.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the method provides for an extract of Brickellia which may be entirely different than the extract of Brickellia which is claimed in claim 1. For example, the method may employ an organic solvent extract, which would have different phytochemical constituents than, say, an aqueous extract. Thus, each extract would necessarily produce different effects when administered to an individual because of their respective phytochemical contents.

Inventions III-VIII are unrelated to each other, or to Inventions I and II. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the Instant case, the Inventions are unrelated in that they may all be practiced separately without practicing another method. For example, the methods for screening a group of compounds for the ability to suppress autoimmune responses in a mammal can be carried out separately, without having to administer any compounds as described in Groups I or VIII because the method could detect totally unrelated compounds. Also, the methods for screening as in Groups VI and VII can be carried out separately from the methods of treating of Groups II-V because, as stated *supra*, the methods if Groups VI and VII may detect unrelated compounds which would be effective for the same ailment. The methods of Groups II and III are unrelated to Group V in that Groups II and III are related to methods for treating diabetes, while Group V is a method for controlling unwanted proliferation to T-cells. Thus, the groups not only employ different compositions, but the etiologies of the ailments are distinct and the methods for treating would be carried out in different manners. Also, Groups II and III are unrelated in that Group II is drawn to a method for treating diabetes comprising an aqueous extract of Brickellia, while Group III is drawn to treating diabetes with luteolin. An aqueous extract of Brickellia would necessarily contain numerous phytochemicals that when administered to an individual would have a different effect than the administration of luteolin alone.

The search for each of the above inventions is not co-extensive particularly with regard to the literature search. Further, a reference which would anticipate the invention of one group would not necessarily anticipate or even make obvious another group.

Because these inventions are distinct for the reasons given above and the search required for each Group is not required for the others, restriction for examination purposes as indicated is proper.

During a telephone conversation with Stefan J. Kirchanski on 8/20/02 a provisional election was made with traverse to prosecute the invention of Group III, claims 8-10. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-7 and 11-17 have been withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 8-10 were presented for examination on the merits.

Priority

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). Thus, the first sentence of the

specification should read; 'This application is a continuation in part of PCT/US00/08957 filed 4/4/2000 which claims benefit of provisional application 60/127,824'.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for treating diabetes via administration of luteolin or quercetin, does not reasonably provide enablement for treatment of diabetes via administration of any other flavanoid or luteolin in combination with other flavonoids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404).

Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Inventions targeted for human therapy bear a heavy responsibility to provide supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The standard of enablement is higher for such inventions because effective treatments for disease conditions are relatively rare, and may be unbelievable in the absence of strong supporting evidence. Claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments.

In the Instant case, Applicants have claimed a method for treating diabetes with flavonoids such as luteolin or quercetin, or luteolin in combination with other flavonoids such as apigenin and dihydrokaemferol for examples. While the Instant specification as filed is fully

enabled for the treatment of diabetes with luteolin and enabled for quercitin since the prior art taught that quercetin had glucose lowering effects (*vide infra*), there is no empirical evidence set forth in the disclosure which would indicate that other flavanoids would also act beneficially *in-vivo* to reduce overall blood glucose levels.

The state of the art is unpredictable. Zarzuelo et al. (1996) for example showed that even a glycoside analog of luteolin, leuteolin 5-O-β-rutinoside, was ineffective in increasing blood insulin levels alone (increase of insulin levels would have inherently decreased blood glucose levels)(Table 1, p.2313). Further unpredictability with regard to the efficacy of closely related flavonoids is evidenced by Okada et al. (1996) and Ammar et al. (1988). Okada et al. demonstrated that flavonoids, although similar in structure, produced varying degrees of pharmaceutical effectiveness with regard to aldose reductase and platelet aggregation *in-vivo* (Table 3). The 27 flavonoids represented in the table showed remarkably different inhibition characteristics, which is clear indication that the flavonoids are unpredictable in nature. Ammar et al. (1988) showed that while quercetin and rutin had blood glucose lowering effects, morin, structurally similar to both quercetin and rutin, did not produce any beneficial results (Tables 1-II, p. 167).

Further, the Instant specification is not enabled for any combination of flavonoids such as luteolin and apigenin for example. First, it is pointed out that the Instant specification merely speculates that flavonoids such as apigenin and dihydrokaemferol were present in the extract: "It

is **believed** that the *Brickellia californica* extract includes the flavonoids dihydrokaemferol, apigenin, luteolin, myricetin and quercetin" (emphasis added) (p. 21, Instant Specification). However, there is no data to support this hypothesis. Thus, the exact phytochemical profile of the final extracted product *is not known*. Although the skilled artisan would necessarily be able to produce a composition comprising the flavonoids of claims 9 and 10 since the flavonoids are obtainable, the skilled artisan would none-the-less be burdened by the task of tedious experimental procedure without expectation of success due to the unpredictable nature of flavonoids, alone and in combination. To practice the instant invention in a manner consistent with the breadth of the claims would not require just a repetition of the work that is described in the instant application but a substantial inventive contribution on the part of a practitioner which would involve the determination of which, if any flavonoids besides luteolin would actually have a positive effect toward blood glucose levels.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, ***he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112***; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons

of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (emphasis added)

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by Ammar et al. (1988). Claim 8 is drawn to a method for lowering blood glucose levels in a diabetic patient via administration of flavonoids such as quercetin.

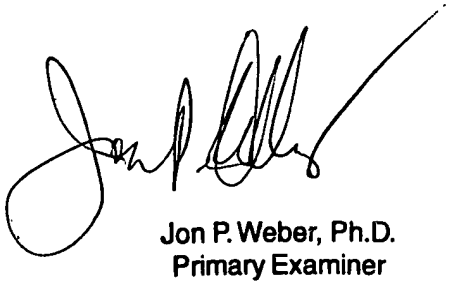
Ammar et al. (1988) disclosed that rats, when administered 200mg/kg of quercetin, displayed reduced blood glucose levels following glucose ingestion (Tables 1 and II, p. 167).

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Patricia Patten, whose telephone number is (703)308-1189. The examiner can normally be reached on M-F from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Jon P. Weber, Ph.D.
Primary Examiner